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PATENT
Attorney Docket No. **DHI-03864**

1643

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	James L. Brown		
Serial No.:	09/539,735	Group No.:	not yet assigned
Filed:	03/30/00	Examiner:	not yet assigned
Entitled:	**DIAGNOSIS OF AUTOIMMUNE DISEASE**		

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: August 7, 2000 By: Anne M. Neiswander

Sir or Madam:

Enclosed please find an Preliminary Amendment, Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. **08-1290**. **An originally executed duplicate of this transmittal is enclosed for this purpose.**

Dated: August 7, 2000

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By: Anne M. Neiswander

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following patent is referred to in the body of the specification:

- U.S. Patent No. 4,609,622, issued Sept. 2, 1986, to Kohn *et al.*.

The following printed publications are referred to in the body of the specification:

- Botero and Brown (1998) "Bioassay of thyrotropin receptor antibodies with Chinese hamster ovary cells transfected with recombinant human thyrotropin receptor: Clinical utility in children and adolescents with Graves disease," J. Pediatr. 132:612-618;
- Federman in *Scientific American Medicine*, Scientific American, New York, NY, Dale and Federman (eds.), 1997, Chptr. 3, Section I, pp. 2-22;
- Baldet *et al.* (1987) "Thyroid stimulating antibody: an index of thyroid stimulation in Graves' disease?"Acta Endocrinol. (Copenh) 116:7-12;

- Rapoport *et al.* (1984) "Clinical Experience with a Human Thyroid Cell Bioassay for Thyroid-Stimulating Immunoglobulin," J. Clin. Endocrinol. Metabol. 58:332-338;
- Yokoyama *et al.* (1987) "Heterogeneity of Graves' Immunoglobulin G: comparison of Thyrotropin Receptor Antibodies in Serum and in Culture Supernatants of Lymphocytes Transformed by Epstein-Barr Virus Infection," J. Clin. Endocrinol. Metabol. 64:215-218;
- McKenzie and Zakarija (1989) "Clinical Review 3, The Clinical Use of Thyrotropin Receptor Antibody Measurements," J. Clin. Endocrinol. Metabol. 69:1093-1096;
- Kasagi *et al.* (1986) "A Sensitive and Practical Assay for Thyroid-Stimulating Antibodies Using Crude Immunoglobulin Fractions Precipitated with Polyethylene Glycol," J. Clin. Endocrinol. Metabol. 62:855-862;
- Bidey *et al.* (1985) "Characterization of thyroid-stimulating immunoglobulin-induced cyclic AMP accumulation in the rat thyroid cell strain FRTL-5: potentiation by forskolin and calibration against reference preparations of thyrotrophin," J. Endocrinol. 105:7-15;
- Michelangeli *et al.* (1994) "Measurement of thyroid stimulating immunoglobulins in a new cell line transfected with a functional human TSH receptor (JPO9 cells), compared with an assay using FRTL-5 cells," Clin. Endocrinol. 40:645-652;
- Kakinuma *et al.*(1997) "The Human Thyrotropin (TSH) Receptor in a TSH Binding Inhibition Assay for TSH Receptor Autoantibodies," J. Clin. Endocrinol. Metabol. 82:2129-2134;
- Vitti *et al.* (1993) "Detection of Thyroid-Stimulating Antibody Using Chinese Hamster Ovary Cells Transfected with Cloned Human Thyrotropin Receptor," J. Clin. Endocrinol. Metabol. 76:499-503;
- Kosugi *et al.* (1989) "Mechanisms by Which Low Salt Condition Increases Sensitivity of Thyroid Stimulating Antibody Assay," Endocrinol. 125:410-417;
- Evans *et al.* (1999) "Development of a Luminescent Bioassay for Thyroid Stimulating Antibodies," J. Clin. Endocrinol. Metabol. 84:374;

- Maniatis *et al.* (1987) "Regulation of Inducible and Tissue-Specific Gene Expression," Science 236:1237-1245;
- Voss *et al.* (1986) "The role of enhancers in the regulation of cell-type-specific transcriptional control," Trends Biochem. Sci. 11:287-289;
- Dijkema *et al.* (1985) "Cloning and expression of the chromosomal immune interferon gene of the rat," EMBO J. 4:761-767;
- Uetsuki *et al.* (1989) "Isolation and Characterizationof the Human Chromosomal Gene for Polypeptide Chain Elongation Factor-1α," J. Biol. Chem. 264:5791-5798;
- Kim *et al.* (1990) "Use of the human elongation factor 1α promoter as a versatile and efficient expression system," Gene 91:217-223;
- Mizushima and Nagata (1990) "pEF-BOS, a powerful mammalian expression vector," Nuc. Acids. Res. 18:5322;
- Gorman *et al.* (1982) "The Rous sarcoma virus long terminal repeat is a strong promoter when introduced into a variety of eukaryotic cells by DNA-mediated transfection," Proc. Natl. Acad. Sci. USA 79:6777-6781;
- Boshart *et al.* (1985) "A Very Strong Enhancer is Located Upstream of am Immediate Early Gene of Human Cytomegalovirus," Cell 41:521-530;
- Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, New York [1989], pp. 16.7-16.8; and
- Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, New York [1989], pp.16.9-16.15.

Applicant has become aware of the following printed publications which may be material to the examination of this application:

- U.S. Patent No. 5,071,773, issued Dec. 10, 1991, to Evans *et al.* Evans *et al.* discloses two hormone receptor-related bioassays. In the first assay, cells which express a test protein that is suspected of being a hormone receptor, and which express a reporter protein under the control of a hormone response promoter/enhancer element are cultured in the presence of a known hormone. Expression of the reporter protein by the cultured cells indicates that the test protein has transcription-activating properties of a hormone receptor. In the

second assay, cells which express a hormone receptor and which express a reporter protein under the control of a hormone response promoter/enhancer element are exposed to a compound which is suspected of being a ligand for the hormone receptor. Expression of the reporter protein indicates that the compound is a ligand to the expressed hormone receptor. In contrast to the claimed invention, Evans *et al.* does not disclose providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol. Evans *et al.* also does not disclose either exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, or observing for the presence of detectable thyroid-stimulating antibodies;

- U.S. Patent No. 5,401,629 issued Mar. 28, 1995 to Harpold *et al.* and U.S. Patent No. 5,436,128 issued Jul. 25, 1995 to Harpold *et al.* Both patents to Harpold *et al.* disclose recombinant cells which express a cell surface protein and which express a reporter gene under the transcriptional control of an element that is responsive to an intracellular signal that is generated by interaction of an agonist with the expressed cell surface protein. The cells of Harpold *et al.* are exposed to a test compound, and observed for changes in the amount of expressed reporter protein relative to a control. Such changes indicate that the test compound is a modulator of the expressed cell surface protein. Unlike the claimed invention, the Harpold *et al.* patents do not disclose providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol. Harpold *et al.*'s patents also do not disclose either exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, or observing for the presence of detectable thyroid-stimulating antibodies;
- Chiovato *et al.* (1994) "Detection of antibodies blocking thyrotropin effect using Chinese hamster ovary cells transfected with the cloned human TSH receptor," J. Endocrinol. Invest. 717:809-816. Chiovato *et al.* discloses an *in*

vitro assay for detecting thyrotropin stimulating hormone-blocking antibodies (TSHBAb) using CHO-R cells and a comparison of the assays when using FRTL-5 cells. CHO-R cells were cultured in RPMI-1640 medium including glutamine, fetal calf serum and geneticin. Cultured cells were then incubated with IgG from human patients, thyroid stimulating hormone (TSH) alone , or both IgG and TSH. TSH stimulation was quantified. Inhibition of TSH stimulation indicated the presence of TSHBAb. Unlike the claimed invention, Chiovato *et al.* does not disclose using polyethylene glycol;

- Di Cerbo *et al.* (1999) "Graves' Immunoglobulins Activate Phospholipase A_2 by Recognizing Specific Epitopes on Thyrotropin Receptor," J. Clin. Endrocinol. Metabol. 84:3283. Di Cerbo *et al.* discloses a method for determining the region in the thyroid-stimulating hormone receptor (TSHR) which contains epitopes for cAMP-stimulating TSHR autoantibodies. The method involves using CHO cells transfected with wild-type hTSHR or with an hTSHR chimera in which residues 8-165 of the hTSHR are substituted by equivalent resides of the LH-CG receptor. Each cell type is incubated with IgG from Graves' patients, and the effect of this incubation on cAMP levels and on adenylyl cyclase (AC) levels is determined. The authors determined that substitution of resides 8-165 of TSHR with homologous residues of LH/CG receptor resulted in a loss of the ability of Graves' IgG to stimulate cAMP production, whereas cAMP signal transduction induced by TSH was preserved. The authors thus concluded that Graves' IgG and TSH require different TSHR domains with respect to AC stimulation. The methods of Di Cerbo *et al.* are distinguished from the instant claims in that Di Cerbo *et al.*'s methods do not utilize polyethylene glycol;
- Guyton (1981) "The Thyroid Hormones," in *Textbook of Medical Physiology*, Sixth Edition, W.B. Saunders Company. Guyton discusses the formation and secretion of thyroid hormones, and hyperthyroidism and hypothyroidism diseases. Unlike the claimed invention, Guyton does not disclose (a) providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol, (b)

exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, and (c) observing for the presence of detectable thyroid-stimulating antibodies;

- Hartmann *et al.* (1993) "The Effects of PEG on Second Antibody Immunoprecipitation and Its Use in Immunoassay," J. Immuno. 14:241-266. Hartmann *et al.* discloses the effect of PEG on the second antibody immunoprecipitation in radioimmunological assays. The assays involved a first step of reacting a first antibody with a radiolabelled antigen or hapten. In the second step, the second antibody and PEG were added to precipitate the antigen-first antibody complexes. Hartmann *et al.*'s assay is distinguished from the claimed methods since Hartmann *et al.* does not use either a test sample suspected of containing thyroid-stimulating autoantibodies, or cultured cells contained within a testing means;
- Inui *et al.* (1998) "Increase of Thyroid Stimulating Activity in Graves' Immunoglobulin-G by High Polyethylene Glycol Concentrations Using Porcine Thyroid Cell Assay," Thyroid 8:319-325. This reference discloses co-incubation of PEG solutions of 0% to 10% with purified thyroid stimulating antibody (TSAB)-immunoglobulin G (IgG) and with cultured porcine thyroid cells (PTC), followed by determination of cAMP levels produced by the cells. Inui *et al.* reported that the maximal increase (approximately 10-fold) in cAMP production was observed with 5% PEG, and that the stimulatory effect of 5% PEG on cAMP production by purified TSAB-IgG occurred in a dose-dependent manner and increased in proportion to the incubation time. However, Inui *et al.* does not disclose providing cultured cells selected from FRTL-5 cells, CHO-R cells, and CHOLuc cells;
- Jacobson *et al.* (1997) "Epidemiology and Estimated Population Burden of Selected Autoimmune Diseases in the United States," Clin. Immunol. and Immunop. 83:223-243. Jacobson *et al.* discloses the results of a study of several autoimmune disorders, including thyroiditis. The study involved estimating the current and future burden (*i.e.*, weighted mean incidence and prevalence rates) of autoimmune diseases in the United States. Unlike the claimed invention,

Jacobson *et al.* does not disclose (a) providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol, (b) exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, and (c) observing for the presence of detectable thyroid-stimulating antibodies;

- Loos *et al.* (1995) "Enhanced cAMP accumulation by the human thyrotropin receptor variant with the Pro52Thr substitution in the extracellular domain," Eur. J. Biochem. 232:62 (Abstract). Loos *et al.* discloses a study of the role of a Pro52Thr substitution in the thyrotropin receptor on the receptor's binding affinity for thyrotropin. cDNA encoding wild-type receptor or receptor which contained the Pro52Thr substitution were stably expressed in Chinese hamster ovary cells. The transformed cells were then exposed to thyrotropin to determine binding affinity and cAMP accumulation. However, Loos *et al.* does not disclose (a) providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol, (b) exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, and (c) observing for the presence of detectable thyroid-stimulating antibodies;
- Ludgate *et al.* (1990) "Use of the recombinant human thyrotropin receptor (TSH-R) expressed in mammalian cell lines to assay TSH-R autoantibodies," Mol. and Cell. Endrocrinol. 73:R13-R18. Ludgate *et al.* discloses generating a CHO cell line (JP26) which is stably transfected with the human TSH-R. This cell line was incubated with IgG preparations from patients with Graves' disease and from normal controls to test the ability of this cell line to detect thyroid stimulating immunoglobulins (TSAb) by increasing its cAMP production. In contrast to the claimed invention, Ludgate *et al.* does not disclose (a) providing polyethylene glycol, or (b) exposing a test sample which is suspected of containing thyroid-stimulating autoantibodies to cultured cells and to polyethylene glycol;

- Ludgate *et al.* (1992) "Recombinant TSH-Receptor for Determination of TSH-Receptor-Antibodies," Exp. Clin. Endocrinol. 100:73-74. Ludgate *et al.* discloses production of two clones, JP09 and JP26, by co-transfection of CHO cells with a pSVL construct containing the coding sequence of human TSH-R and with a pSV2neo. The stably transfected JP09 and JP26 clones were selected for high levels of expression of TSH-R. The JP26 clone was incubated with IgGs from normal subjects or patients and the levels of cAMP were determined. The Ludgate *et al.* method is distinguished from the claimed methods in that it does not include either providing polyethylene glycol, or exposing a test sample which is suspected of containing thyroid-stimulating autoantibodies to cultured cells and to polyethylene glycol;
- McKenzie and Zakarija (1985) "Assays of Thyroid-Stimulating Antibody," Methods in Enzymol. 109:677-691. This reference reviews methods for the measurement of thyroid-stimulating antibody (TSAb) of Graves' disease, including methods which utilize guinea pig fat cell membranes, human thyroid membranes, human thyroid tissue slices, human thyroid cells in monolayer culture, and functioning rat thyroid cells (FRTL cells). However, this reference does not disclose using polyethylene glycol in any of these methods;
- Morgenthaler *et al.* (1998) "Application of a bioassay with CHO cells for the routine detection of stimulating and blocking autoantibodies to the TSH-receptor," Horm. Metab. Res. 30:162, Abstract. Morgenthaler *et al.* discloses a modified method for detection of thyroid stimulating autoantibodies (TSAb) which uses JP09 CHO cells and unfractionated human serum. The method of Morgenthaler *et al.* is distinguished from the claimed methods in that it does not use polyethylene glycol;
- Murakami *et al.* (1995) "Clinical usefulness of thyroid-stimulating antibody measurement using Chinese hamster ovary cells expressing human thyrotropin receptors," Euro. J. Endocrinol. 133:80-86. Murakami *et al.* discloses the generation of CHO-hTSH-R cells which are CHO cells that express human TSH receptors. These cells were incubated with IgG of patients with Graves' disease and Hashimoto's thyroiditis. The results were compared with a

conventional thyroid-stimulating antibody (TS-Ab) assay using porcine thyroid cells and a TSH-binding inhibiting immunoglobulin (TBII) assay. Unlike the claimed methods, Murakami *et al.*'s methods do not involve using polyethylene glycol;

- Ochi *et al.* (1999) "Clinical Usefulness of TSAb Assay with High Polyethylene Glycol Concentrations," Horm. Res. 51:142-149. Ochi *et al.* expands on the experiments described *supra* by Inui *et al.* in connection with the stimulatory effect of PEG on TSAb-IgG-stimulated cAMP production in porcine thyroid cells (PTC). Ochi *et al.* discloses incubating cultured PTC with (a) untreated test sera from Graves' disease patients and 5% PEG, and (b) crude γ-globulin precipitated by 12.5% PEG (PEG 12.5% PF) or by 22.5% PEG (PEG 22.5% PF) from Graves' sera in the absence and presence of different concentrations of PEG. Incubation is followed by determining cAMP production by the PTC. Ochi *et al.* reported that cAMP production by the untreated test serum was significantly increased by the addition of 5% PEG. Ochi *et al.* also disclosed that the PEG 12.5% PF + 4% PEG method and the PEG 22.5% PF method were suitable for assaying TSAb. However, Ochi *et al.* does not disclose providing cultured cells selected from FRTL-5 cells, CHO-R cells, and CHOLuc cells;
- Perret *et al.* (1990) "Stable Expression of the Human TSH Receptor in CHO Cells and Characterization of Differentially Expressing Clones," Biochem. Biophys. Res. Comm. 171:1044-1050. Perre *et al.* reports the stable expression of the human thyrotropin receptor (hTSHr) in CHO cells and characterization of individual clones expressing different levels of the hTSHr. Clones were tested for their cAMP response to antibodies from a patient with high levels of thyroid stimulating antibodies. In contrast to the claimed method, Perre *et al.* does not disclose using polyethylene glycol;
- Persani *et al.* (1993) "Measurement of cAMP accumulation in Chinese hamster ovary cells transfected with the recombinant human TSH receptor (CHO-R): a new bioassay for human thyrotropin," J. Endocrinol. Invest. 16:511-519. Persani *et al.* discloses an assay based on cAMP accumulation in CHO cells

transfected with recombinant human TSH receptor (CHO-R). The assay involved incubating the cells with recombinant human TSH, bovine TSH, untreated sera from human subjects, or with human sera from which TSH was partially purified by immunoaffinity separation. Persani *et al.* is distinguished from the claimed invention since it does not disclose using polyethylene glycol;

- Roitt *et al.* (1998) Immunology, Fifth Edition, Mosby International Ltd., pp 371-380. Roitt *et al.* reviews the principles underlying the clinical immunology and pathogenicity of autoantibodies, and the diagnostic and prognostic value of autoantibodies. However, Roitt *et al.* does not disclose providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol. Roitt *et al.* also does not disclose either exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, or observing for the presence of detectable thyroid-stimulating antibodies;
- Saito *et al.* (1989) "Enhancement of the Activity of Thyroid-Stimulating Antibodies by Anti-Human IgG Antibodies *In Vitro*," Clin. Endrocrinol. 31:325-334. Saito *et al.* discloses incubating FRTL-5 cells with Graves' disease IgG in the presence and absence of anti-human IgG antibodies, followed by determination of the level of cAMP accumulation in the medium. The method of Saito *et al.* is distinguished from the claimed methods in that it does not include using polyethylene glycol;
- Smith *et al.* (1988) "Autoantibodies to the Thyrotropin Receptor," Endocrine Reviews 9:106-121. Smith *et al.* reviews methods for detecting thyrotropin receptor autoantibodies (TRAb), including the use of detergent-solubilized TSH receptors from thyroid membranes, and of bioassays employing isolated thyroid cells from human or porcine tissue, and the rat thyroid cell line $FRTL_5$. Smith *et al.*, however, does not disclose using polyethylene glycol;
- Vitti *et al.* (1988) "Measurement of TSAb directly in serum using FRTL-5 Cells," J. Endocrinol. Invest. 11:313-317. Vitti *et al.* evaluated whether whole serum instead of purified IgG could be used for the detection of TSAb using

FRTL-5 cells. Vitti *et al.* discloses that it is possible to measure TSAb directly in serum using FRTL-5 cells, although the assay is less sensitive than when using purified IgG. The method of Vitti *et al.* is contrasted with the claimed methods in that Vitti *et al.* does not disclose using polyethylene glycol;

- Wallaschofski and Peschke (1999) "Detection of thyroid stimulating (TSAB)- and thyrotropin stimulation blocking (TSBAB) antibodies with CHO cell lines expressing different TSH-receptor numbers," Clin. Endocrinol. 50:365-372. This reference discloses optimization of the CHO cell bioassay conditions for detection of TSHR antibodies in patients with Graves' disease. Optimization included determining the effect of the number of hTSHR expressed per cell, cell number per well, and serum dilution. Nonetheless, this reference does not disclose using polyethylene glycol;
- Watson *et al.* (1998) "A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease," Clin. Endo. 49:577-581. Watson *et al.* discloses a chemiluminescent assay for the detection of TSAb in serum samples from Graves' disease patients. A CHO cell line, which is stably transformed with a reporter plasmid containing the firefly luciferase gene under the transcriptional control of multiple cAMP responsive elements (CRE), was transfected with the human thyroid stimulating hormone (TSH) receptor. The resulting NA-4 clonal line was incubated with patients' sera and intracellular cAMP levels were determined. Unlike the claimed invention, Watson *et al.*'s method does not employ using polyethylene glycol;
- Yamashiro *et al.* (1999) "Mechanism of the Augmentative Effect of High Polyethylene Glycol (PEG) Concentrations on the Thyroid Stimulating Activity in TSAb-IgG Using a Porcine Thyroid Cell Assay," Endocrine Research 25:67-75. Yamashiro *et al.* investigated the mechanism underlying the results which are described *supra* by Inui et al. in connection with the stimulatory effect of 5% PEG on TSAb-IgG-stimulated cAMP production in porcine thyroid cells (PTC). Yamashiro *et al.* used a two-step incubation with PTC. In the fist step, protein A-purified TSAb-IgG and PTC were pre-incubated with or without 5% PEG. In the second step, the pre-incubated PTC were reincubated with fresh

buffer. cAMP levels were measured intracellularly and in the culture medium after the first and second steps. Yamashiro *et al.* reports that the augmentation effect of 5% PEG on cAMP production by TSAb-Ag was observed whenever 5% PEG and TSAb-IgG were co-incubated in either the first or second incubation. Yamashiro *et al.* concludes that the stimulatory effect of 5% PEG on TSAb-IgG-stimulated cAMP production may be due to the increase of binding or incorporation of TSAb-IgG into the membranes of PTC compared to TSH. However, Yamashiro *et al.* does not disclose providing cultured cells selected from FRTL-5 cells, CHO-R cells, and CHOLuc cells;

- FAQ Information: FAQ on Graves' Disease (1999) http//www.geocities.com/Athens/3626/graves.html. This document discusses Graves' disease, its symptoms, diagnosis, and treatment. However, it does not disclose (a) providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol, (b) exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, and (c) observing for the presence of detectable thyroid-stimulating antibodies; and
- FAQ about Graves' Disease (1999) http://www.ngdf.org/faq.htm. This document outlines the symptoms and treatment of Graves' disease. However, it does not disclose (a) providing a test sample suspected of containing thyroid-stimulating autoantibodies, cultured cells contained within a testing means, and polyethylene glycol, (b) exposing the test sample to the cultured cells and to the polyethylene glycol under conditions such that the thyroid-stimulating antibodies are detectable, and (c) observing for the presence of detectable thyroid-stimulating antibodies.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: 7 August 2000

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